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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,638	11/14/2000	Isidore Rigoutsos	YOR920000435US1	8850

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EXAMINER

LY, CHEYNE D

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 09/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/712,638	RIGOUTSOS ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12,23 and 25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12,23 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. In view of the Appeal Brief filed on July 21, 2004, PROSECUTION IS HEREBY REOPENED. New grounds of rejections are set forth below.

2. The finality of the instant Office Action has been withdrawn.

3. To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

4. If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

5. Applicant's arguments presented in said Appeal Brief have been addressed below. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

6. Claims 1-12, 23, and 25, are examined on the merits.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claims 4 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Specific to the limitation of “without using any knowledge about properties or features of sequences”, said limitation causes claim 4, which depends from claim 1, to be vague and indefinite because claim 1 recites “the sequences are not aligned.” The recitation of “the sequences are not aligned” in claim 1 has been reasonably construed as providing “knowledge about properties or features of sequences.” Therefore, the step of discovering without “knowledge about properties or features of sequences” in claim 4 is unclear since “knowledge about properties or features of sequences” has been previously provided in claim 1. Clarification of the metes and bounds is required.

10. Specific to line 2, the limitation of “unaligned sequences” causes claim 4 to be vague and indefinite because claim 1, line 2, from which claim 4 depends, recites “not aligned.” Claim 4 is unclear whether the limitations are the same. Further, the antecedent basis for said limitations are unclear because of the inconsistency of said limitations. Clarification of the metes and bounds is required.

11. Claim 7, lines 1-2, the limitation of “for one of the positions...one expected symbol is a plurality of expected symbols” causes said claim to be vague and indefinite because it is unclear whether “one of the positions” is occupied by one symbol or a plurality of symbols. Clarification of the metes and bounds is required.

CLAIM REJECTIONS - 35 USC § 101

12. 35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 1-12, 23, and 25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory algorithm type subject matter.

14. The instant rejection is directed to the computer embodiment of the claimed invention.

15. Claims 1-12, 23, and 25 are rejected because said claims are directed to a method, system, and an article of manufacture comprising steps for analyzing sequence data without any physical alteration step, which is considered to be non-statutory subject matter. "For example, a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing the mathematical algorithm is statutory" (MPEP § 2106 (IV)(B)(2) (b), part ii). Similar to the nonstatutory example above, the instant invention comprises algorithmic steps for analyzing sequence data without any physical alteration resulted from said analysis.

16. It is acknowledged that claims 23 and 25 are directed to a system and an article of manufacture comprising computer components for processing sequence data. However, the processing steps achieved by said computer components do not cause any physical alteration outside of the system or article of manufacture resulted from said processes. Therefore, the processes performed by the system or article of manufacture are "not determinative of whether the process is statutory because such transformation alone does not distinguish a statutory computer process from a nonstatutory computer process" (MPEP § 2106 (IV)(B)(2) (b), part ii).

CLAIM REJECTIONS UNDER - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-8, 10-12, 23 and 25 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Benson et al. (1997).

RESPONSE TO ARGUMENTS

19. Applicant arguments have been fully considered and responded to via the citation of inherent support from the newly cited secondary references.

ART REJECTION

20. Benson et al. discloses that the NCBI provides GenBank comprising over 600 million nucleotide bases, and a subset of GenBank is the UniGene collection of unique human gene sequences (Benson et al., page 1, column 2, Organization of the database §, and page 2, column 2, EST data §, lines 16-18).

21. The inclusion of NCBI News is not being used as prior art, but only to expand on the inherent characteristics of the UniGene Collection as cited by Benson et al. NCBI News discloses UniGene comprises clusters of EST sequences wherein said EST sequences are not complete and have not been characterized (unaligned), as in instant claim 4. ESTs are screened against each other to determine those likely to be derived from the same gene and sequences share statistically significant DNA similarity (common patterns) are placed into the same cluster, as in instant claim 5. One important use of the UniGene clusters (set of sequences) is to identify novel and non-redundant sequence candidates that identifies coding sequences in the genome based on predetermined patterns of said clusters (NCBI News, page 3, lines 1-35), as in instant claims 1-3.

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22. The UniGene set serves as a source of mapping candidates and as a standard to compare and screen new EST submissions. ESTs are screened against each other to determine those likely to be derived from the same gene and sequences share statistically significant (predetermined threshold) DNA similarity (common patterns), and placed into the same cluster (NCBI News, page 3, lines 1-35). New EST submissions that do not match any sequences (predetermined threshold) in the UniGene set are considered (selected) new human genes and are organized into unique clusters to provide additional mapping candidates (NCBI News, page 3, last line, to page 4, line 3), as in instant claims 8 and 11.

23. UniGene screens all ESTs against existing functionally cloned GenBank entries to eliminate redundancies (NCBI News, page 3, lines 35-36). In this manner, the nearly 500,000 ESTs in dbEST have been reduced 10-fold to ~50,000 sequence clusters (create a new set of sequences) to be used for gene discovery (Benson et al., page 2, column 2, EST data §), as in instant claim 10.

24. “NCBI offers the BLAST family of search programs to perform fast searching with rigorous statistical methods for judging the significance of matches” (Benson et al., Page 5, column 1, lines 42-44). The inclusion of a reference by Altschul et al. is not being used as prior art, but only to expand on the inherent characteristics of BLAST as cited above.

25. In BLAST, statistical significance scores are calculated a set of probabilities for the occurrence of individual residues (at least one expected symbol), and for aligning pairs of residues (plurality of positions) (Altschul et al., page 405, column 2, §3. Results). BLAST measures well-defined mutation scores (occupied by any sequence character) and detects

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biologically significant sequence similarities (Altschul et al., page 404, column 1, lines 1-9), as in instant claim 6 and 7.

26. The choice of word length and threshold parameters determines the probability of hits yielded wherein hits are sequences with common patterns. If no common patterns are detected, the choice of word length and threshold parameters may be decreased to increase the probability of finding hits (common patterns) (Altschul et al., pages 406-408, The choice of word length and threshold parameters §), as in instant claim 12.

27. GenBank is a part of the Entrez system (Abstract etc.). "The server/client version of Entrez operates with a client program on a user's machine over the Internet connected to a server located at NCBI. Client programs for Macintosh, PC and UNIX computers can be obtained by downloading from 'ncbi.nlm.nih.gov' (Benson et al., Page 5, column 1, lines 26-30), the above disclosures anticipate the limitations of claims 23 and 25.

CLAIM REJECTIONS - 35 USC § 103

28. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

29. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

30. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benson et al. (1997) taken with Kleffe et al. (1998).

31. Benson et al. discloses the limitations to claims 1-8 and 10-12 as discussed above.

Further, Benson et al. discloses GenBank comprising *Arabidopsis* sequences (page 2, column 1, line 1) is a major source of sequences for new gene discoveries (Benson et al., page 2, EST data §).

32. However, Benson et al. does not disclose the limitation of using a second-order Markov chain method.

33. Kleffe et al. discloses an improvement for using second-order Markov chain method to predict gene structure (Abstract etc.). The method of Kleffe et al. requires the use of GenBank sequence information (page 233, column 1, Derivation of gene structures §). The second-order Markov chain method is used to determine the natural logarithm of the probability of a specific sequence (pattern) occur in the *Arabidopsis* sequences (pages 242-243, Appendix: Derivation of Markov models §), as in instant claim 9.

34. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement disclosed by Kleffe et al. and utilize the second-order Markov chain method in the method of Benson et al. for discovering new genes. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to

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use the gene discovery method of Benson et al. and Kleffe et al. with the second-order Markov chain method.

CONCLUSION

35. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

36. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

37. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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38. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

39. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

C. Dune Ly
9/23/04

Ardin H. Marschel 9/26/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER